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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/508,254 | 10/02/2000 | Marc F. Charette | CIBT-P01-558 | 9598 |

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ROPES & GRAY
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER

DEBERRY, REGINA M

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 11/12/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/508,254

Applicant(s)

CHARETTE ET AL.

Examiner

Regina M. DeBerry

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 20 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13, 15-23 and 25-29 is/are pending in the application.
- 4a) Of the above claim(s) 2-10, 12 and 25-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 11, 13, 15-23, 28 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

Status of Application, Amendments and/or Claims

The amendment filed 02 May 2002 (Paper No. 12) has been entered in full. The amendment filed 20 August 2002 (Paper No. 14) has been entered in full. Claim 24 was cancelled.

Applicant has stated that the instant response combines the contents of the original unsigned reply/amendment of Paper No. 12 and the content of the signed supplemental amendment filed on 03 May 2002. Claims 1, 11, 13, 15-23, 28 and 29 are under examination.

Priority under 35 U.S.C 119(e) has been met.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The objection to the specification as set forth on page 3 of the previous Office Action (27 October 2001, Paper No. 8) is *withdrawn* in view of the amendment (20 August 2002, Paper No. 14).

The objection of claims 11, 13, 18, 19 and 23 as set forth at page 4 of the previous Office Action (27 October 2001, Paper No. 8) is *withdrawn* in view of the amendment (20 August 2002, Paper No. 14).

The rejection of claims 1, 11, 13, 15-23 under 35 U.S.C 102(a) as being anticipated by Bengtsson *et al.* as set forth at pages 9-10 of the previous Office Action (27 October 2001, Paper No. 8) is *withdrawn* in view of the amendment (20 August 2002, Paper No. 14).

The rejection of claims 28 and 29 under 35 U.S.C 103(a) as being unpatentable over Lein *et al.*, in view of Durbec *et al.* and Weiss *et al.* as set forth at pages 12-13 of the previous Office Action (27 October 2001, Paper No. 8) is *withdrawn* in view of the amendment (20 August 2002, Paper No. 14).

Claim Rejections - 35 USC § 112, first paragraph scope of enablement

Claims 28 and 29 are rejected under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such as way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pages 3-5 of the previous Office Action (15 June 2001, Paper No. 13).

Applicant's arguments have been fully considered but not deemed persuasive for the following reasons.

Applicant states that in the case of the present invention, there is no sound reason to question that the claimed treatment methods would be efficacious in an *in vivo* model. Applicant cites the MPEP 2164 and Cross v. Iizuka to support arguments. Applicant states that the evidence presented demonstrates that the methods of the present invention have broad applicability. The MPEP, however, states that if there is no correlation, then the examples do not constitute working examples. In Cross v. Iizuka, the compounds in question had been subjected to both *in vitro* and *in vivo* testing. Claims 28 and 29 are drawn to pharmaceuticals for promoting the survival or growth of mammalian neural cells and the inhibition of death or degeneration of mammalian cells.

In the instant specification, there is no correlation between the *in vitro* effect of survival/outgrowth in peripheral ganglia and a pharmaceutical having the activity of promoting survival, growth or inhibition of death or degeneration of any type of mammalian neural cell in the body (*in vivo*). In addition, claim 29 is not enabled for the property of inhibiting death or degeneration because the instant examples disclose an effect of enhanced process formation, which is different for inhibition of death or degeneration.

Thus the scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 103

Claims 1, 11, 13 and 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lein *et al.* in view of Durbec *et al.* The basis for this rejection is set forth at pages 10-12 of the previous Office Action (15 June 2001, Paper No. 13).

Applicant's arguments have been fully considered but not deemed persuasive for the following reasons.

Applicant states that Durbec does not teach or suggest any equivalence between NGF and GDNF as contended by the Examiner, nor does the Examiner cite any other evidence in the art to establish a structural equivalence between GDNF and NGF. Applicant cites Durbec, stating the GDNF signals through a receptor tyrosine kinase (RTK) while other members of the TGF- β superfamily signal through serine-threonine kinase receptors.

Durbec states that "because other members of the TGF- β family of growth factors signal through serine-threonine kinase receptors, it is intriguing that GDNF signals through an RTK". "We believe that this emphasizes further the distant relationship of GDNF to other members of this family of growth factors, and raises the possibility that additional molecules similar to TGF- β could bind to and activate RTKs". "However, we cannot exclude the possibility that GDNF also binds to and signals through additional serine-threonine kinase receptors" (page 792). The specification states that NGF and GDNF are tropic factors that have been shown to enhance the survival and differentiation of dopaminergic neurons in tissue culture (page 3, lines 5-10). In addition, the instant specification and the claims recite tropic factors GDNF and NGF as "GDNF/NGF". Lastly, NGF also signals through receptor tyrosine kinases, OP/BMP signals through serine/kinase receptors (specification, lines 19-20).

Thus the scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, first paragraph scope of enablement

Claims 1, 13, 15-23 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement because the specification while being enabling for a method for promoting survival or outgrowth of mammalian peripheral ganglia *in vitro*, wherein said cells express an OP/BMP-activated serine/threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor comprising contacting mammalian peripheral ganglia with an effective concentration of a preparation comprising

(a) OP-1 morphogen having an amino acid sequence having at least 70% homology with the C-terminal seven cysteine skeleton of human OP-1 wherein said OP/BMP morphogen can induce ectopic bone, and

(b) a GDNF/NGF neurotrophic factor selected from GDNF and NT-3, does not reasonable provide enablement for promoting survival or growth of mammalian neural cells.

There are hundreds of different types of neural cells. The instant specification specifically teaches the survival or outgrowth of peripheral ganglia, not any mammalian neural cell (specification, page 22, lines 4-30). Neural cells encompass neurons in the central nervous system (CNS). Jackowski teaches the difference between damage to the peripheral nervous system (PNS) and the CNS and theories, which address the causes of regeneration failure in mammalian CNS. In addition, the specification teaches the survival or outgrowth of peripheral ganglia in the presence of OP-1 and NT-3 or OP-1 and GDNF, not any OP/BMP morphogen or GDNF/NGF neurotrophic factor (specification, page 22, lines 25-30). Lastly, the survival/outgrowth effects disclosed were *in vitro*. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Due to the large quantity of experimentation necessary to demonstrate growth and survival in various types of mammalian neural cells, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the contradictory state of the prior art which teaches away from new growth or regeneration in the CNS, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowed.

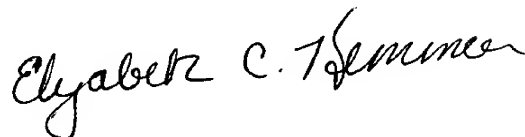
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



RMD
October 23, 2002



ELIZABETH KEMMERER
PRIMARY EXAMINER